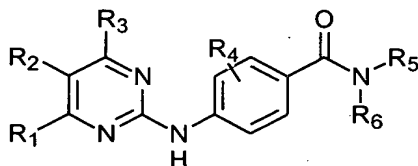


What is claimed is:

1. A method for treating a condition responsive to inhibition of the JNK pathway, comprising administering to a patient in need thereof and effective amount of a compound having the structure:



or a pharmaceutically acceptable salt thereof,  
wherein:

R<sub>1</sub> is aryl or heteroaryl optionally substituted with one to four substituents independently selected from R<sub>7</sub>;

R<sub>2</sub> and R<sub>3</sub> are the same or different and are independently hydrogen or lower alkyl;

R<sub>4</sub> represents one to four optional substituents, wherein each substituent is the same or different and independently selected from halogen, hydroxy, lower alkyl or lower alkoxy;

R<sub>5</sub> and R<sub>6</sub> are the same or different and independently -R<sub>8</sub>, -(CH<sub>2</sub>)<sub>α</sub>C(=O)R<sub>9</sub>, -(CH<sub>2</sub>)<sub>α</sub>C(=O)OR<sub>9</sub>, -(CH<sub>2</sub>)<sub>α</sub>C(=O)NR<sub>9</sub>R<sub>10</sub>, -(CH<sub>2</sub>)<sub>α</sub>C(=O)NR<sub>9</sub>(CH<sub>2</sub>)<sub>b</sub>C(=O)R<sub>10</sub>, -(CH<sub>2</sub>)<sub>α</sub>NR<sub>9</sub>C(=O)R<sub>10</sub>, -(CH<sub>2</sub>)<sub>α</sub>NR<sub>11</sub>C(=O)NR<sub>9</sub>R<sub>10</sub>, -(CH<sub>2</sub>)<sub>α</sub>NR<sub>9</sub>R<sub>10</sub>, -(CH<sub>2</sub>)<sub>α</sub>OR<sub>9</sub>, -(CH<sub>2</sub>)<sub>α</sub>SO<sub>c</sub>R<sub>9</sub>, or -(CH<sub>2</sub>)<sub>α</sub>SO<sub>2</sub>NR<sub>9</sub>R<sub>10</sub>;

or R<sub>5</sub> and R<sub>6</sub> taken together with the nitrogen atom to which they are attached to form a heterocycle or substituted heterocycle;

R<sub>7</sub> is at each occurrence independently halogen, hydroxy, cyano, nitro, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, heterocycle, substituted heterocycle, heterocyclealkyl, substituted heterocyclealkyl, -C(=O)OR<sub>8</sub>, -OC(=O)R<sub>8</sub>, -C(=O)NR<sub>8</sub>R<sub>9</sub>, -C(=O)NR<sub>8</sub>OR<sub>9</sub>, -SO<sub>c</sub>R<sub>8</sub>, -SO<sub>c</sub>NR<sub>8</sub>R<sub>9</sub>, -NR<sub>8</sub>SO<sub>c</sub>R<sub>9</sub>, -NR<sub>8</sub>R<sub>9</sub>, -NR<sub>8</sub>C(=O)R<sub>9</sub>, -NR<sub>8</sub>C(=O)(CH<sub>2</sub>)<sub>b</sub>OR<sub>9</sub>, -NR<sub>8</sub>C(=O)(CH<sub>2</sub>)<sub>b</sub>R<sub>9</sub>, -O(CH<sub>2</sub>)<sub>b</sub>NR<sub>8</sub>R<sub>9</sub>, or heterocycle fused to phenyl;

R<sub>8</sub>, R<sub>9</sub>, R<sub>10</sub> and R<sub>11</sub> are the same or different and at each occurrence

independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl or substituted heterocyclealkyl;

or R<sub>8</sub> and R<sub>9</sub> taken together with the atom or atoms to which they are attached to form a heterocycle or substituted heterocycle;

*a* and *b* are the same or different and at each occurrence independently selected from 0, 1, 2, 3 or 4; and

*c* is at each occurrence 0, 1 or 2.

2. The method of claim 1 wherein the condition is an inflammatory or autoimmune condition.

3. The method of claim 2 wherein the inflammatory or autoimmune condition is rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gout, asthma, bronchitis, allergic rhinitis, chronic obstructive pulmonary disease, cystic fibrosis, inflammatory bowel disease, irritable bowel syndrome, mucous colitis, ulcerative colitis, Crohn's disease, gastritis, esophagitis, hepatitis, pancreatitis, nephritis, psoriasis, eczema, dermatitis, multiple sclerosis, Lou Gehrig's disease, sepsis, conjunctivitis, acute respiratory distress syndrome, purpura, nasal polip or lupus erythematosus.

4. The method of claim 1 wherein the condition is a cardiovascular, metabolic or ischemic condition.

5. The method of claim 4 wherein the condition is atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy, Type II diabetes, osteoporosis, erectile dysfunction, cachexia, myocardial infraction, ischemic diseases of heart, kidney, liver, and brain, organ transplant rejection, graft versus host disease, endotoxin shock, or multiple organ failure.

6. The method of claim 1 wherein the condition is an infectious disease.

7. The method of claim 6 wherein the infectious disease is a viral infection.

8. The method of claim 7 wherein the viral infection is caused by human

immunodeficiency virus, hepatitis B virus, hepatitis C virus, human papillomavirus, human T-cell leukemia virus or Epstein-Barr virus.

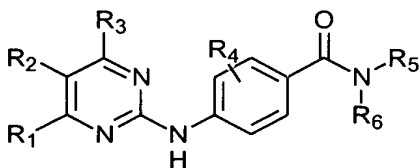
9. The method of claim 1 wherein the condition is cancer.

10. The method of claim 9 wherein the cancer is of the colon, rectum, prostate, liver, lung, bronchus, pancreas, brain, head, neck, stomach, skin, kidney, cervix, blood, larynx, esophagus, mouth, pharynx, testes, urinary bladder, ovary or uterus.

11. The method of claim 1 wherein the condition is stroke, epilepsy, Alzheimer's disease or Parkinson's disease.

12. The method of claim 9 further comprising administering an effective amount of a cytotoxic agent or radiation therapy.

13. A method for treating an inflammatory or an autoimmune condition comprising administering to a patient in need thereof an effective amount of a compound having the structure:



or a pharmaceutically acceptable salt thereof,

wherein:

R<sub>1</sub> is aryl or heteroaryl optionally substituted with one to four substituents independently selected from R<sub>7</sub>;

R<sub>2</sub> and R<sub>3</sub> are the same or different and are independently hydrogen or lower alkyl;

R<sub>4</sub> represents one to four optional substituents, wherein each substituent is the same or different and independently selected from halogen, hydroxy, lower alkyl or lower alkoxy;

R<sub>5</sub> and R<sub>6</sub> are the same or different and independently -R<sub>8</sub>, -(CH<sub>2</sub>)<sub>α</sub>C(=O)R<sub>9</sub>,  
-(CH<sub>2</sub>)<sub>α</sub>C(=O)OR<sub>9</sub>, -(CH<sub>2</sub>)<sub>α</sub>C(=O)NR<sub>9</sub>R<sub>10</sub>,  
-(CH<sub>2</sub>)<sub>α</sub>C(=O)NR<sub>9</sub>(CH<sub>2</sub>)<sub>β</sub>C(=O)R<sub>10</sub>, -(CH<sub>2</sub>)<sub>α</sub>NR<sub>9</sub>C(=O)R<sub>10</sub>,

$-(CH_2)_\alpha NR_{11}C(=O)NR_9R_{10}$ ,  $-(CH_2)_\alpha NR_9R_{10}$ ,  $-(CH_2)_\alpha OR_9$ ,  
 $-(CH_2)_\alpha SO_cR_9$ , or  $-(CH_2)_\alpha SO_2NR_9R_{10}$ ;

or  $R_5$  and  $R_6$  taken together with the nitrogen atom to which they are attached to form a heterocycle or substituted heterocycle;

$R_7$  is at each occurrence independently halogen, hydroxy, cyano, nitro, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, heterocycle, substituted heterocycle, heterocyclealkyl, substituted heterocyclealkyl,  $-C(=O)OR_8$ ,  $-OC(=O)R_8$ ,  $-C(=O)NR_8R_9$ ,  $-C(=O)NR_8OR_9$ ,  $-SO_cR_8$ ,  $-SO_cNR_8R_9$ ,  $-NR_8SO_cR_9$ ,  $-NR_8R_9$ ,  $-NR_8C(=O)R_9$ ,  $-NR_8C(=O)(CH_2)_bOR_9$ ,  $-NR_8C(=O)(CH_2)_bR_9$ ,  $-O(CH_2)_bNR_8R_9$ , or heterocycle fused to phenyl;

$R_8$ ,  $R_9$ ,  $R_{10}$  and  $R_{11}$  are the same or different and at each occurrence independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl or substituted heterocyclealkyl;

or  $R_8$  and  $R_9$  taken together with the atom or atoms to which they are attached to form a heterocycle or substituted heterocycle;

$a$  and  $b$  are the same or different and at each occurrence independently selected from 0, 1, 2, 3 or 4; and

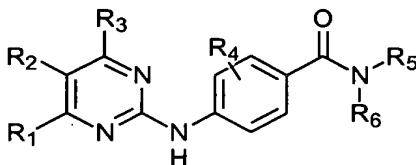
$c$  is at each occurrence 0, 1 or 2.

14. The method of claim 13 further comprising administering an effective amount of an anti-inflammatory agent.

15. The method of claim 14, wherein the anti-inflammatory agent is salicylic acid, acetylsalicylic acid, methyl salicylate, diflunisal, salsalate, olsalazine, sulfasalazine, acetaminophen, indomethacin, sulindac, etodolac, mefenamic acid, meclofenamate sodium, tolmetin, ketorolac, dichlofenac, ibuprofen, naproxen, naproxen sodium, fenoprofen, ketoprofen, flurbiprofen, oxaprozin, piroxicam, meloxicam, ampiroxicam, droxicam, pivoxicam, tenoxicam, nabumetone, phenylbutazone, oxyphenbutazone, antipyrine, aminopyrine, apazone and nimesulide, zileuton, aurothioglucose, gold sodium thiomalate, auranofin, colchicine, allopurinol, probenecid, sulfinpyrazone, benzbromarone, enbrel, infliximab, anakinra, celecoxib or rofecoxib.

16. The method of claim 13, wherein the inflammatory or autoimmune condition is rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gout, asthma, bronchitis, allergic rhinitis, chronic obstructive pulmonary disease, cystic fibrosis, inflammatory bowel disease, irritable bowel syndrome, mucous colitis, ulcerative colitis, Crohn's disease, gastritis, esophagitis, hepatitis, pancreatitis, nephritis, psoriasis, eczema, dermatitis, multiple sclerosis, Lou Gehrig's disease, sepsis, conjunctivitis, acute respiratory distress syndrome, purpura, nasal polip or lupus erythematosus.

17. A method for treating a cardiovascular, metabolic or ischemic condition comprising administering to a patient in need thereof an effective amount of a compound having the structure:



or a pharmaceutically acceptable salt thereof,

wherein:

R<sub>1</sub> is aryl or heteroaryl optionally substituted with one to four substituents independently selected from R<sub>7</sub>;

R<sub>2</sub> and R<sub>3</sub> are the same or different and are independently hydrogen or lower alkyl;

R<sub>4</sub> represents one to four optional substituents, wherein each substituent is the same or different and independently selected from halogen, hydroxy, lower alkyl or lower alkoxy;

R<sub>5</sub> and R<sub>6</sub> are the same or different and independently -R<sub>8</sub>, -(CH<sub>2</sub>)<sub>α</sub>C(=O)R<sub>9</sub>, -(CH<sub>2</sub>)<sub>α</sub>C(=O)OR<sub>9</sub>, -(CH<sub>2</sub>)<sub>α</sub>C(=O)NR<sub>9</sub>R<sub>10</sub>, -(CH<sub>2</sub>)<sub>α</sub>C(=O)NR<sub>9</sub>(CH<sub>2</sub>)<sub>b</sub>C(=O)R<sub>10</sub>, -(CH<sub>2</sub>)<sub>α</sub>NR<sub>9</sub>C(=O)R<sub>10</sub>, -(CH<sub>2</sub>)<sub>α</sub>NR<sub>11</sub>C(=O)NR<sub>9</sub>R<sub>10</sub>, -(CH<sub>2</sub>)<sub>α</sub>NR<sub>9</sub>R<sub>10</sub>, -(CH<sub>2</sub>)<sub>α</sub>OR<sub>9</sub>, -(CH<sub>2</sub>)<sub>α</sub>SO<sub>c</sub>R<sub>9</sub>, or -(CH<sub>2</sub>)<sub>α</sub>SO<sub>2</sub>NR<sub>9</sub>R<sub>10</sub>;

or R<sub>5</sub> and R<sub>6</sub> taken together with the nitrogen atom to which they are attached to form a heterocycle or substituted heterocycle;

R<sub>7</sub> is at each occurrence independently halogen, hydroxy, cyano, nitro, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, substituted aryl, aralkyl, substituted

aralkyl, heterocycle, substituted heterocycle, heterocyclealkyl, substituted heterocyclealkyl,  $-C(=O)OR_8$ ,  $-OC(=O)R_8$ ,  $-C(=O)NR_8R_9$ ,  $-C(=O)NR_8OR_9$ ,  $-SO_cR_8$ ,  $-SO_cNR_8R_9$ ,  $-NR_8SO_cR_9$ ,  $-NR_8R_9$ ,  $-NR_8C(=O)R_9$ ,  $-NR_8C(=O)(CH_2)_bOR_9$ ,  $-NR_8C(=O)(CH_2)_bR_9$ ,  $-O(CH_2)_bNR_8R_9$ , or heterocycle fused to phenyl;

$R_8$ ,  $R_9$ ,  $R_{10}$  and  $R_{11}$  are the same or different and at each occurrence independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl or substituted heterocyclealkyl;

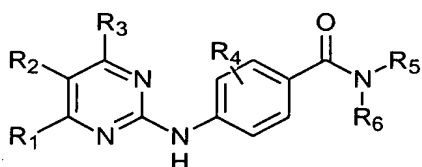
or  $R_8$  and  $R_9$  taken together with the atom or atoms to which they are attached to form a heterocycle or substituted heterocycle;

$a$  and  $b$  are the same or different and at each occurrence independently selected from 0, 1, 2, 3 or 4; and

$c$  is at each occurrence 0, 1 or 2.

18. The method of claim 17, wherein the condition is atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy, Type II diabetes, osteoporosis, erectile dysfunction, cachexia, myocardial infarction, ischemic diseases of heart, kidney, liver, and brain, organ transplant rejection, graft versus host disease, endotoxin shock, or multiple organ failure.

19. A method for treating an infectious disease comprising administering to a patient in need thereof an effective amount of a compound having the structure:



or a pharmaceutically acceptable salt thereof,

wherein:

$R_1$  is aryl or heteroaryl optionally substituted with one to four substituents independently selected from  $R_7$ ;

$R_2$  and  $R_3$  are the same or different and are independently hydrogen or lower alkyl;

$R_4$  represents one to four optional substituents, wherein each substituent is

the same or different and independently selected from halogen,  
hydroxy, lower alkyl or lower alkoxy;

$R_5$  and  $R_6$  are the same or different and independently  $-R_8$ ,  $-(CH_2)_aC(=O)R_9$ ,  
 $-(CH_2)_aC(=O)OR_9$ ,  $-(CH_2)_aC(=O)NR_9R_{10}$ ,  
 $-(CH_2)_aC(=O)NR_9(CH_2)_bC(=O)R_{10}$ ,  $-(CH_2)_aNR_9C(=O)R_{10}$ ,  
 $-(CH_2)_aNR_{11}C(=O)NR_9R_{10}$ ,  $-(CH_2)_aNR_9R_{10}$ ,  $-(CH_2)_aOR_9$ ,  
 $-(CH_2)_aSO_cR_9$ , or  $-(CH_2)_aSO_2NR_9R_{10}$ ;

or  $R_5$  and  $R_6$  taken together with the nitrogen atom to which they are  
attached to form a heterocycle or substituted heterocycle;

$R_7$  is at each occurrence independently halogen, hydroxy, cyano, nitro,  
carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl,  
sulfonylalkyl, hydroxyalkyl, aryl, substituted aryl, aralkyl, substituted  
aralkyl, heterocycle, substituted heterocycle, heterocyclealkyl,  
substituted heterocyclealkyl,  $-C(=O)OR_8$ ,  $-OC(=O)R_8$ ,  $-C(=O)NR_8R_9$ ,  
 $-C(=O)NR_8OR_9$ ,  $-SO_cR_8$ ,  $-SO_cNR_8R_9$ ,  $-NR_8SO_cR_9$ ,  $-NR_8R_9$ ,  $-$   
 $NR_8C(=O)R_9$ ,  $-NR_8C(=O)(CH_2)_bOR_9$ ,  $-NR_8C(=O)(CH_2)_bR_9$ ,  
 $-O(CH_2)_bNR_8R_9$ , or heterocycle fused to phenyl;

$R_8$ ,  $R_9$ ,  $R_{10}$  and  $R_{11}$  are the same or different and at each occurrence  
independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl,  
aralkyl, substituted arylalkyl, heterocycle, substituted heterocycle,  
heterocyclealkyl or substituted heterocyclealkyl;

or  $R_8$  and  $R_9$  taken together with the atom or atoms to which they are  
attached to form a heterocycle or substituted heterocycle;

$a$  and  $b$  are the same or different and at each occurrence independently  
selected from 0, 1, 2, 3 or 4; and

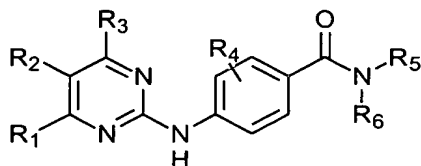
$c$  is at each occurrence 0, 1 or 2.

20. The method of claim 19 wherein the infectious disease is a viral  
infection.

21. The method of claim 20 wherein the viral infection is caused by  
human immunodeficiency virus, hepatitis B virus, hepatitis C virus, human papillomavirus,  
human T-cell leukemia virus or Epstein-Barr virus.

22. A method for treating cancer comprising administering to a patient in

need thereof an effective amount of a compound having the structure:



or a pharmaceutically acceptable salt thereof,

wherein:

R<sub>1</sub> is aryl or heteroaryl optionally substituted with one to four substituents independently selected from R<sub>7</sub>;

R<sub>2</sub> and R<sub>3</sub> are the same or different and are independently hydrogen or lower alkyl;

R<sub>4</sub> represents one to four optional substituents, wherein each substituent is the same or different and independently selected from halogen, hydroxy, lower alkyl or lower alkoxy;

R<sub>5</sub> and R<sub>6</sub> are the same or different and independently -R<sub>8</sub>, -(CH<sub>2</sub>)<sub>α</sub>C(=O)R<sub>9</sub>, -(CH<sub>2</sub>)<sub>α</sub>C(=O)OR<sub>9</sub>, -(CH<sub>2</sub>)<sub>α</sub>C(=O)NR<sub>9</sub>R<sub>10</sub>, -(CH<sub>2</sub>)<sub>α</sub>C(=O)NR<sub>9</sub>(CH<sub>2</sub>)<sub>b</sub>C(=O)R<sub>10</sub>, -(CH<sub>2</sub>)<sub>α</sub>NR<sub>9</sub>C(=O)R<sub>10</sub>, -(CH<sub>2</sub>)<sub>α</sub>NR<sub>11</sub>C(=O)NR<sub>9</sub>R<sub>10</sub>, -(CH<sub>2</sub>)<sub>α</sub>NR<sub>9</sub>R<sub>10</sub>, -(CH<sub>2</sub>)<sub>α</sub>OR<sub>9</sub>, -(CH<sub>2</sub>)<sub>α</sub>SO<sub>c</sub>R<sub>9</sub>, or -(CH<sub>2</sub>)<sub>α</sub>SO<sub>2</sub>NR<sub>9</sub>R<sub>10</sub>;

or R<sub>5</sub> and R<sub>6</sub> taken together with the nitrogen atom to which they are attached to form a heterocycle or substituted heterocycle;

R<sub>7</sub> is at each occurrence independently halogen, hydroxy, cyano, nitro, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, heterocycle, substituted heterocycle, heterocyclealkyl, substituted heterocyclealkyl, -C(=O)OR<sub>8</sub>, -OC(=O)R<sub>8</sub>, -C(=O)NR<sub>8</sub>R<sub>9</sub>, -C(=O)NR<sub>8</sub>OR<sub>9</sub>, -SO<sub>c</sub>R<sub>8</sub>, -SO<sub>c</sub>NR<sub>8</sub>R<sub>9</sub>, -NR<sub>8</sub>SO<sub>c</sub>R<sub>9</sub>, -NR<sub>8</sub>R<sub>9</sub>, -NR<sub>8</sub>C(=O)R<sub>9</sub>, -NR<sub>8</sub>C(=O)(CH<sub>2</sub>)<sub>b</sub>OR<sub>9</sub>, -NR<sub>8</sub>C(=O)(CH<sub>2</sub>)<sub>b</sub>R<sub>9</sub>, -O(CH<sub>2</sub>)<sub>b</sub>NR<sub>8</sub>R<sub>9</sub>, or heterocycle fused to phenyl;

R<sub>8</sub>, R<sub>9</sub>, R<sub>10</sub> and R<sub>11</sub> are the same or different and at each occurrence independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl or substituted heterocyclealkyl;

or R<sub>8</sub> and R<sub>9</sub> taken together with the atom or atoms to which they are



attached to form a heterocycle or substituted heterocycle;  
*a* and *b* are the same or different and at each occurrence independently  
selected from 0, 1, 2, 3 or 4; and  
*c* is at each occurrence 0, 1 or 2.

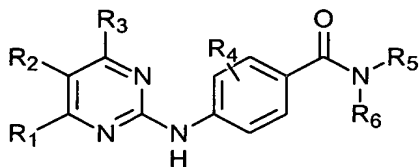
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23. The method of claim 22 further comprising administering an effective amount of an anti-cancer agent.

24. The method of claim 23 wherein the anti-cancer agent is  
10 cyclophosphamide, Ifosfamide, trofosfamide, Chlorambucil, carmustine (BCNU), Lomustine (CCNU), busulfan, Treosulfan, Dacarbazine, Cisplatin, carboplatin, vincristine, Vinblastine, Vindesine, Vinorelbine, paclitaxel, Docetaxol, etoposide, Teniposide, Topotecan, 9-aminocamptothecin, camptoirinotecan, crisnatol, mytomyacin C, methotrexate, Trimetrexate, mycophenolic acid, Tiazofurin, Ribavirin, EICAR, hydroxyurea, deferoxamine, 5-  
15 fluorouracil, Floxuridine, Doxifluridine, Ratitrexed, cytarabine (ara C), cytosine arabinoside, fludarabine, mercaptopurine, thioguanine, Tamoxifen, Raloxifene, megestrol, goserclin, Leuprolide acetate, flutamide, bicalutamide, B 1089, CB 1093, KH 1060, vertoporphin (BPD-MA), Phthalocyanine, photosensitizer Pc4, demethoxyhypocrellin A (2BA-2-DMHA), interferon- $\alpha$ , interferon- $\gamma$ , tumor-necrosis factor, Lovastatin, 1-methyl-4-phenylpyridinium  
20 ion, staurosporine, Actinomycin D, Dactinomycin, bleomycin A2, Bleomycin B2, Peplomycin, daunorubicin, Doxorubicin (adriamycin), Idarubicin, Epirubicin, Pirarubicin, Zorubicin, Mitoxantrone, verapamil or thapsigargin.

25. The method of claim 22 wherein the cancer is of the colon, rectum, prostate, liver, lung, bronchus, pancreas, brain, head, neck, stomach, skin, kidney, cervix, blood, larynx, esophagus, mouth, pharynx, testes, urinary bladder, ovary or uterus.

26. A method for treating stroke, epilepsy, Alzheimer's disease, or Parkinson's disease comprising administering to a patient in need thereof an effective  
30 amount of a compound having the structure:



35

or a pharmaceutically acceptable salt thereof,

wherein:

$R_1$  is aryl or heteroaryl optionally substituted with one to four substituents independently selected from  $R_7$ ;

$R_2$  and  $R_3$  are the same or different and are independently hydrogen or lower alkyl;

$R_4$  represents one to four optional substituents, wherein each substituent is the same or different and independently selected from halogen, hydroxy, lower alkyl or lower alkoxy;

$R_5$  and  $R_6$  are the same or different and independently  $-R_8$ ,  $-(CH_2)_aC(=O)R_9$ ,  $-(CH_2)_aC(=O)OR_9$ ,  $-(CH_2)_aC(=O)NR_9R_{10}$ ,  $-(CH_2)_aC(=O)NR_9(CH_2)_bC(=O)R_{10}$ ,  $-(CH_2)_aNR_9C(=O)R_{10}$ ,  $-(CH_2)_aNR_{11}C(=O)NR_9R_{10}$ ,  $-(CH_2)_aNR_9R_{10}$ ,  $-(CH_2)_aOR_9$ ,  $-(CH_2)_aSO_cR_9$ , or  $-(CH_2)_aSO_2NR_9R_{10}$ ;

or  $R_5$  and  $R_6$  taken together with the nitrogen atom to which they are attached to form a heterocycle or substituted heterocycle;

$R_7$  is at each occurrence independently halogen, hydroxy, cyano, nitro, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, heterocycle, substituted heterocycle, heterocyclealkyl, substituted heterocyclealkyl,  $-C(=O)OR_8$ ,  $-OC(=O)R_8$ ,  $-C(=O)NR_8R_9$ ,  $-C(=O)NR_8OR_9$ ,  $-SO_cR_8$ ,  $-SO_cNR_8R_9$ ,  $-NR_8SO_cR_9$ ,  $-NR_8R_9$ ,  $-NR_8C(=O)R_9$ ,  $-NR_8C(=O)(CH_2)_bOR_9$ ,  $-NR_8C(=O)(CH_2)_bR_9$ ,  $-O(CH_2)_bNR_8R_9$ , or heterocycle fused to phenyl;

$R_8$ ,  $R_9$ ,  $R_{10}$  and  $R_{11}$  are the same or different and at each occurrence independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl or substituted heterocyclealkyl;

or  $R_8$  and  $R_9$  taken together with the atom or atoms to which they are attached to form a heterocycle or substituted heterocycle;

$a$  and  $b$  are the same or different and at each occurrence independently selected from 0, 1, 2, 3 or 4; and

$c$  is at each occurrence 0, 1 or 2.